PTO/SB/17 (01-03)
Approved for use through 04/30/2003. OMB 0651-0032

FEE TRANSMITTAL for FY 2003

Patent fees are subject to annual revision.

Complete if Known	
Application Number	09/241636
Filing Date	February 2, 1999
First Named Inventor	Ellen M. Heath
Examiner Name	Not Yet Assigned
Group Art Unit	N/A
Attorney Docket No.	GSIM-P01-006

[X] Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 840.00

METHOD OF PAYMENT *(check all that apply)*

[ ] Check [ ] Credit Card [ ] Money Order [ ] Other [ ] None

[X] Deposit Account

Deposit Account Number: 18-1945

Deposit Account Name: Ropes & Gray LLP

The Commissioner is hereby authorized to: *(check all that apply)*

[X] Charge fee(s) indicated below [X] Credit any overpayments

[X] Charge any additional fee(s) during the pendency of this application

[ ] Charge fee(s) indicated below, **except for the filing fee**

to the above-identified deposit account.

FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1001	750	2001	375	Utility filing fee	
1002	330	2002	165	Design filing fee	
1003	520	2003	260	Plant filing fee	
1004	750	2004	375	Reissue filing fee	
1005	160	2005	80	Provisional filing fee	

SUBTOTAL (1) ($) 0.00

2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

	Extra Claims		Fee from below		Fee Paid
Total Claims		-** =		x =	
Independent Claims		-** =		x =	
Multiple Dependent				=	

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
1202	18	2202	9	Claims in excess of 20
1201	84	2201	42	Independent claims in excess of 3
1203	280	2203	140	Multiple dependent claim, if not paid
1204	84	2204	42	** Reissue independent claims over original patent
1205	18	2205	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) ($) 0.00

***or number previously paid, if greater; For Reissues, see above*

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1051	130	2051	65	Surcharge – late filing fee or oath	
1052	50	2052	25	Surcharge – late provisional filing fee or cover sheet.	
1053	130	1053	130	Non-English specification	
1812	2,520	1812	2,520	For filing a request for *ex parte* reexamination	
1804	920*	1804	920*	Requesting publication of SIR prior to Examiner action	
1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action	
1251	110	2251	55	Extension for reply within first month	
1252	410	2252	205	Extension for reply within second month	
1253	930	2253	465	Extension for reply within third month	465.00
1254	1,450	2254	725	Extension for reply within fourth month	
1255	1,970	2255	985	Extension for reply within fifth month	
1401	320	2401	160	Notice of Appeal	
1402	320	2402	160	Filing a brief in support of an appeal	
1403	280	2403	140	Request for oral hearing	
1451	1,510	1451	1,510	Petition to institute a public use proceeding	
1452	110	2452	55	Petition to revive – unavoidable	
1453	1,300	2453	650	Petition to revive - unintentional	
1501	1,300	2501	650	Utility issue fee (or reissue)	
1502	470	2502	235	Design issue fee	
1503	630	2503	315	Plant issue fee	
1460	130	1460	130	Petitions to the Commissioner	
1807	50	1807	50	Processing fee under 37 CFR 1.17(q)	
1806	180	1806	180	Submission of Information Disclosure Stmt	
8021	40	8021	40	Recording each patent assignment per property (times number of properties)	
1809	750	2809	375	Filing a submission after final rejection (37 CFR 1.129(a))	
1810	750	2810	375	For each additional invention to be examined (37CFR 1.129(b))	
1801	750	2801	375	Request for Continued Examination (RCE)	375.00
1802	900	1802	900	Request for expedited examination of a design application	
Other fee (specify)					

*Reduced by Basic Filing Fee Paid **SUBTOTAL (3)** ($) 840.00

SUBMITTED BY				Complete *(if applicable)*	
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Signature				*Date*	June 6, 2003

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Group Art Unit: 1655
Examiner: Jeanine Enewold Goldberg

In Re Application of:
Inventor(s) : Ellen M. Heath *et al.*

Serial No. : 09/241,636

Filed : February 2, 1999

For : PROCESSES FOR ISOLATING, AMPLIFYING AND CHARACTERIZING DNA

Attorney Docket No. : 5253

RESPONSE TO OFFICE ACTION

Assistant Commissioner of Patents
Washington, D.C. 20231

RESPONSE

This is a response to the outstanding final office action, dated December 6, 20022. A petition for a three month extension of time, up to and including June 6, 2003 and a Request for Continued Examination accompanies this response.

35 USC 103

Item 5. The Examiner states that "[c]laims 1-3, 5-6, 11-21, 23-30, 32-33, 37, 39, 41, 45-51, 53-56, 58, 60-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boom et al (5,234,809) in view of Shieh (US Pat. 6,054,039, April 2000)."

The Examiner rebutted the arguments filed on September 19, 2002. The applicant wishes to maintain the arguments stated in the response filed on September 19,2002 as well as clarify points raised in these arguments.

First, the applicant wishes to reiterate that Boom teaches that "it is essential to use a chaotropic substance" such as guanidinium (iso)thiocyanate and guanidinium hydrochloride, and urea. See Boom, Col. 3, lines 56-67. Also, see Boom, Claim 3. Thus, the process according to Boom requires the use of highly toxic chaotropic substances such as the aforementioned chaotropes. While the claims of the present invention are not restricted to non-chaotropic substances, it is stated in the specification that the invention seeks to avoid the use of such toxic substances. Indeed, what distinguishes the present invention from the prior art is Therefore, the applicant would be amenable to restricting the claims of the invention to the use of non-toxic non-chaotropic substances such as guanidinium (iso)thiocyanate and guanidinium hydrochloride, and urea.

Furthermore, it is respectfully pointed out to the Examiner that the applicant specifically pointed out that Boom teaches the use of an excess of lysing reagent in ***solution*** in which the solid support and biological material were suspended. Boom specifically teaches that sufficiently large amounts of chaotropes are to be mixed with the biological material (for example in a chaotrope:biological material ratio of 1:18) and then mixed with the solid support (beads). Thus, although Boom teaches the combination of a lysing reagent (chaotrope), solid support (beads) and nucleic acid sample, Boom specifically teaches the combination of an excess of chaotropic lysing reagent to enable complete lysis of the biological sample. In this situation, the biological material is primarily lysed in the excess solution of the highly chaotropic mixture,

the DNA released into the solution, which due to the mixing process is then bound to the solid support. It is inconceivable to concentrate already high concentrations of Guanidinium salt in solution and immobilize it on the surface of the solid support. Thus, the lysing must be conducted in solution under the conditions described in Boom.

The Examiner states that Shieh is being relied upon [in this 103 rejection] for the teachings that lysing reagents, generally, may be dried upon a solid support and allow lysis. The Examiner also goes on to state that the ordinary artisan would have been motivated to have prepared the pre-treated lysing membrane of Shieh, for use in the method of Boom, and that the skilled artisan would have had a reasonable expectation of success for analyzing DNA from a solid support that was pretreated with a lysing reagent since Boom teaches a method in which all three components, a lysing reagent, solid support and nucleic acid sample, were contacted with successful results.

It is respectfully pointed out to the Examiner, that according to the method disclosed in Boom "it is essential to use a chaotropic substance" such as guanidinium (iso)thiocyanate and guanidinium hydrochloride, and urea. See Boom, Col. 3, lines 56-67. Also, see Boom, Claim 3. Thus, the process according to Boom requires the use of highly toxic chaotropic substances such as the aforementioned chaotropes. Sufficiently large amounts of chaotropes are mixed with the biological material (for example in a chaotrope:biological material ratio of 1:18). Thus, although Boom teaches the combination of a lysing reagent (chaotrope), solid support (beads) and nucleic acid sample, Boom specifically teaches the combination of an excess of chaotropic lysing reagent to enable complete lysis of the biological sample.

Shieh on the other hand teaches conditions in which the lysis of red blood cells will occur. Shieh teaches that a membrane may be treated with any agent used in the art to cause lysis of red blood cells (See Shieh, Col 10, line 67 to Col 11, line 1). Thus, Shieh teaches that the membrane was dipped in a solution of a surfactant such as 2% Mega-8 and dried to achieve the purpose of lysing red blood cells. The cell lysing component of Shieh is defined to be one that causes disruption of the cellular structure such that a determination of total glycoprotein can be made (See Shieh, Col. 14, lines 21-22). The conditions described in Example 3. B that the Examiner relies upon to assert that Shieh teaches lysis of whole blood are identical to those in which Shieh teaches the lysis of red blood cells. Taking the aforementioned teachings of Shieh into account as a whole, one skilled in the art would believe that when Shieh states that the "lysis of whole blood" occurs, Shieh is specifically referring to the cellular lysis of red blood cells in which the cellular membrane is disrupted to release glycosylated proteins and hemoglobin. It is reiterated in this response that nowhere in the entire specification or claims does Shieh mention lysis of the cells to cause the binding of nucleic acids to the solid support. The conditions that Shieh teaches are wholly related to the preferential rupture of red blood cellsin whole blood. Nowhere does Shieh teach or suggest that the conditions in which a "lysing reagent" as defined by Shieh would result in cell lysis of the sort contemplated by either the instant invention or Boom. Furthermore, it would be impossible to concentrate high concentrations of chaotropic substances such as guanidinium and urea onto the surface of a solid support without causing serious problems such as salting out and caking. The Examiner is reminded that substances such as guanidium and urea must be used at such high concentrations as 6M in solution to cause lysis. When, however, these substances are used at very low concentrations, they tend to cause cell adhesion and binding, and are often components of cell culture solutions.

When an obviousness determination relies on the combination of two or more references, there must be some suggestion or motivation to combine the references. The Examiner is assuming that one skilled in the art could apply the same conditions used in Boom in which a strongly chaotropic lysing reagent is used in excess to cause lysis to that taught in Shieh in which a surfactant is provided at conditions to cause the disrupture of red blood cells. The fact that Boom requires a chaotrope in excess to cause lysis teaches away from applying a very small fractional amount of that lysing reagent to a membrane to cause lysis. The Examiner's assertion that Shieh is being relied upon to promote the idea that lysing reagents in general can be applied to membranes to cause lysis of cells such as to release DNA is an over-reaching assumption because Shieh does not provide such a teaching. Furthermore, the teachings of Boom in which an excess of chaotrope is mandated to cause lysis teach away from the Examiner's assertion.

Item 6. The Examiner states that "[c]laims 1-20, 24-33, 37-41, 44-49, 54-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deggerdal (WO 96/18731) in view of Shieh (US Pat. 6,054,039, April 2000)."

The aforementioned discussions detailing the differences between the instant invention and the inventions of Boom and Shieh overcome this rejection cited by the Examiner. Furthermore, Deggerdal teaches the same method as Boom does in which the solid support, biological material and lysing reagent are mixed together such that there is an excess of lysing reagent to assist in lysing.

Item 7. The Examiner states that "[c]laims 38 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boom (5,234,809) in view of Shieh (US Pat. 6,054,039, April 2000) as applied to Claims 1-3, 5-6, 11-21, 23-30, 32-33, 37, 39, 41, 45-51, 53-56, 58, 60-62 above, and further in view of in view of Deggerdal (WO 96/18731)."

The aforementioned discussions detailing the differences between the instant invention and the inventions of Boom and Shieh overcome this rejection cited by the Examiner.

Item 8. The Examiner states that "[c]laims 23 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deggerdal (WO 96/18731) in view of Shieh (US Pat. 6,054,039, April 2000) as applied to Claims 1-20, 24-33, 37-41, 44-49, 54-62 above and further in view of Boom (5,234,809)."

The aforementioned discussions detailing the differences between the instant invention and the inventions of Boom and Shieh overcome this rejection cited by the Examiner.

Item 9. The Examiner states that "[c]laims 7, 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boom (5,234,809) in view of Shieh (US Pat. 6,054,039, April 2000) as applied to Claims 1-3, 5-6, 11-21, 23-30, 32-33, 37, 39, 41, 45-51, 53-56, 58, 60-62 above and further in view of Su (5,804,684)."

The aforementioned discussions detailing the differences between the instant invention and the inventions of Boom and Shieh overcome this rejection cited by the Examiner.

Item 10. The Examiner states that "[c]laims 42-43 are rejected under 35 U.S.C. 104(a) as being unpatentable over Boom (5,804,684) in view of Shieh (US Pat. 6,054,039, April 2000) as

applied to Claims 1-3, 5-6, 11-21, 23-30, 32-33, 37, 39, 41, 45-51, 53-56, 58, 60-62 above or Deggerdal (WO 96/18731) in view of Shieh (US Pat. 6,054,039, April 2000) as applied to Claims 1-20, 24-33, 37-41, 44-49, 54-62 above and further in view of Su (5,804684)."

The aforementioned discussions detailing the differences between the instant invention and the inventions of Boom and Shieh overcome this rejection cited by the Examiner.

Item 11. The Examiner states that "[c]laims 22 and 51-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boom (5,804,684) in view of Shieh (US Pat. 6,054,039, April 2000) as applied to Claims 1-3, 5-6, 11-21, 23-30, 32-22, 37, 39, 41, 45-51, 53-56, 58, 60-62 above or Deggerdal (WO 96/18731) in view of Shieh (US Pat. 6,054,039), April 2000) as applied to Claims 1-20, 24-33, 37-41, 44-49, 54-62 above and further in view of Sambrook (Molecular Cloning)."

The aforementioned discussions detailing the differences between the instant invention and the inventions of Boom and Shieh overcome this rejection cited by the Examiner.

Item 12. The Examiner states that "[c]laims 33 and 35-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boom (5,804,684) in view of Shieh (US Pat. 6,054,039, April 2000) as applied to Claims 1-3, 5-6, 11-21, 23-30, 32-33, 37, 39, 41, 45-51, 53-56, 58, 60-62 above or Deggerdal (WO 96/18731) in view of Shieh (US Pat. 6,054,039, April 2000) as applied to Claims 1-20, 24-33, 37-41, 44-49, 54-62 above and further in view of Arnold (5,599,667)."

The aforementioned discussions detailing the differences between the instant invention and the inventions of Boom and Shieh overcome this rejection cited by the Examiner.

Item 13. The Examiner states that "[c]laims 34 is rejected under 35 U.S.C. 103(a) as being unpatentable over Boom (5,804,684) in view of Shieh (US Pat. 6,054,039, April 2000) or Deggerdal (WO 96/18731) in view of Shieh (US Pat. 6,054,039, April 2000) and further in view of Arnold (5,599,6667) as applied to claim 33, 35-36 above, and further in view of Hasebe (5,151,345).

The aforementioned discussions detailing the differences between the instant invention and the inventions of Boom and Shieh overcome this rejection cited by the Examiner.

Based on the amendments and remarks above, applicants believe that all pending claims are in condition for allowance.

If the Examiner believes that a conference would be of value in expediting the prosecution of this application, the Examiner is hereby invited to telephone undersigned counsel to arrange for such a conference.

Respectfully submitted,

Dated: June 6, 2003

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